Editorial Manager(tm) for International Journal of Cardiovascular Imaging
Manuscript Draft

Manuscript Number: CAIM368R1

Title: Effects of Steady State Free Precession Parameters on Cardiac Mass, Function, and Volumes

Article Type: Original Article

Section/Category:

Keywords: Interslice gap; Magnetic resonance imaging; Slice thickness; Temporal resolution; Ventricular function

Corresponding Author: Dr Steffen Erhard Petersen, M.D., D.Phil

Corresponding Author's Institution: University of Oxford

First Author: Steffen Erhard Petersen, M.D., D.Phil

Order of Authors: Steffen Erhard Petersen, M.D., D.Phil; Maureen C Hogan, MD, MSc, BSc; Steffen E Petersen, MD, DPhil; Lucy E Hudsmith, MA, MRCP; Jane M Francis, DCCR, DNM; Stefan Neubauer, MD, FRCP

Manuscript Region of Origin:

Abstract: Purpose. We aimed to investigate comparability of LV volumes, function, and mass acquired with three steady-state free precession (SSFP) pulse sequences, simulating typical vendor and protocol specific differences in data acquisition.
Methods. Twenty-one healthy subjects (11 male and 10 female; age range 23-49) underwent cardiac magnetic resonance (CMR) imaging at 1.5 Tesla (T). A complete stack of short-axis views covering the entire left ventricle (LV) were acquired for each of the three SSFP sequences, differing in the interslice gap and slice thickness (7mm with no gap (7/0mm); 7mm with a 3mm gap (7/3mm) and 6mm with a 4mm gap (6/4mm)) with slight variations in acquisition parameters. For each sequence, the LV volumes, function, and mass were determined. Intra- and inter-observer variability and inter-study reproducibility were assessed for all protocols.

Results. All LV volumes, function and mass parameters were similar for the three SSFP sequences ($p>0.05$ for all). The LV ejection fraction for the 7/3 mm sequence was 67.2 ± 6.0, 67.4 ± 5.3 for the 7/0mm sequence, and the 6/4 mm sequence was 69.2 ± 5.7. The LV mass ranged from 119.8 ± 32.4 for the 7/3 mm sequence to 122.2 ± 34.0 for the 7/0 mm sequence. Variabilities were low with no difference in variability between the sequences.

Conclusion. The three SSFP pulse sequence techniques resulted in similar LV volume, function, and mass measurements with no difference in observer and interstudy variabilities. This may allow application and transfer of LV volume studies and databases based on different imaging parameters, at different CMR sites, with a given post-processing method. Future multi-centre studies may now be in a position to consider multi-vendor study designs for LV volume studies.

Comments from Reviewer #1:

We would like to thank the reviewer for his/her thoughtful comments. In the revised version, we have incorporated all suggestions. We feel that this has considerably strengthened the manuscript.

This paper describes the effect of relatively small variations in MRI SSFP pulse sequence upon calculated cardiac functional parameters. The authors show that results from different groups may be compared if the applies pulse sequence does not vary too much. This is an interesting result.

Questions:

Relatively large differences in observed LV-mass appear (intraobserver) from the Bland-Altman plot. Please comment on this in the discussion section. A major difference in the pulse sequence 6/4 as compared to the others is the pixel size: in plane resolution 1.5x1.5mm versus ~1.9x1.5mm; this should be noted in the discussion section, it might have consequences for the quantitative results.

Response:

The intra-observer variability for LV mass was found to be in the range of 4.2% (6/4 mm technique) to 5.8% (7/0 mm technique). These are acceptable values for intra-observer variabilities and agree with many published studies applying cardiac magnetic resonance imaging for determination of LV mass.

We have added the following sentence to the second paragraph in the discussion: “The lower spatial resolution of the 6/4 mm technique (1.9 x 1.5 mm) compared to the other two techniques (1.5 x 1.5 mm) may also contribute to the observed trend for differences in LV end-systolic volume and ejection fraction.”

Comments from Reviewer #2:

We would like to thank the reviewer for his/her thoughtful comments. In the revised version, we have incorporated all suggestions. We feel that this has considerably strengthened the manuscript.

The authors present the results of a study comparing LV volumes, function, and mass acquired with three steady-state free precession (SSFP) pulse sequences. Their main findings include

- All LV volumes, function and mass parameters were similar for the three SSFP sequences ($p>0.05$ for all)

- Variabilities were low with no difference in variability between the sequences. The authors conclude that their findings may allow application and transfer of LV volume studies and databases based on different imaging parameters at different CMR sites, and that future multi-centre studies may now be in a position to consider multivendor study designs for LV volume studies.

General Comments

1. What was the reason to believe that the results from the different protocols would vary significantly? The hypothesis (page 2) seems awkward.

Response: The main aim of our study was to investigate whether there would be clinically relevant differences among the LV volume results based on three different MR sequences. Work in this area with sequences that differ more than ours (i.e. ref [3] Moon, and ref [6] Kunz et al.) do find differences, and so it is not obvious that we would find no difference between these more similar approaches. As we were not expecting significant differences, we have now altered our hypothesis in the introduction as follows:
"We hypothesized there would not be a significant difference among the three SSFP pulse sequence techniques**."**

2. The cardiology community has lived with fairly poor interobserver and intraindividual variability of echo measures but this has never hindered anybody to use echocardiography to measure LV function in multicenter trials. In addition, in clinical trials the effect of measurement variability on sample size is small compared to the effect of expected difference between treatment groups.
Response: We entirely agree with the reviewer that echocardiography with poorer observer variability has been widely used in multicentre trials. This was mainly due to the low cost of echo studies and the widespread availability of echo machines. However, recent studies suggest that due to the markedly reduced variability in determination of LV mass, LV volumes etc using cardiac MRI sample size for multicentre studies can be dramatically reduced by up to 97% depending on the parameter of interest (Bellenger NG et al, J Cardiovasc Magn Reson; 2000;2(4):271-8). This may lead to an actual reduction in the cost of multicentre trials. So for a given expected difference between treatment groups, the improved variability of cardiac MRI allows a substantial reduction of sample size.

3. The study group consisted of young patients, who were lean, and had a low heart rate. Left ventricular morphology was normal in all, and the range of ejection fraction was very narrow. This limits the generalizability of the authors' findings to patients with (severe) cardiovascular disease and abnormal heart rhythms, LV geometry and ejection fractions.
Response: This is a very valuable comment. We have added a sentence of caution to our discussion to extrapolate these findings to diseased hearts. We would hope that given the coverage of the entire heart, geometric assumptions are minimal and would not lead to relevant differences among the three sequences.
Our conclusion now reads as follows:
"We have shown the LV volume, function, and mass parameters acquired at 1.5T using three SSFP pulse sequence techniques in healthy controls are comparable and interchangeable. This finding is particularly important for patients receiving care in different geographical locations and may allow multi-centre trials to include multiple vendor CMR centers, optimizing patient recruitment. However, future studies may need to confirm our findings in patients with dilated or hypertrophied hearts."

Specific Comments

1. Page 4, para 3: "... even small differences in cardiac parameters can influence patient treatment and prognosis." From a clinician's perspective this is not true. If you want to keep this sentence, should provide a reference that supports the "small differences" notion.

Response: We agree that the prognosis of a patient does not change significantly with minor changes in ejection fraction. We have therefore changed this sentence in the introduction accordingly. However, we feel that clinical management decisions are based on rather arbitrary cut-off values and therefore minor changes can alter patient management, e.g. in the indication for implantable cardioverter defibrillators or cardiac re-synchronisation therapy. We have therefore added an example to the introduction which now reads as follows:

"From a clinical perspective, it is critically important that results obtained from different CMR machines and from various manufacturers are interchangeable as even small differences in cardiac parameters can influence patient treatment, e.g Implantable cardioverter defibrillator indications are partly based on cut-off values for ejection fraction of less than 30 or 35%."

2. Please explain your methods in more detail. It is ultimately not clear whether each examiner imaged only a few patients and analyzed their images (I suspect this is the case based on your description of analyzing interobserver variability), or if all examiners were involved with the analysis of all studies from all patients. What was the rationale for your study design?

Response: We apologize that this has not been clear enough. Essentially, three examiners JMF, LEH and SEP performed the MR investigations. The whole dataset, including the repeat scans for interstudy reproducibility, was analyzed by MEH who also re-analyzed the images for intra-observer variability. JMF analyzed the data for inter-observer variability.

We changed our methods section and hope that this now clarifies this further:

"The inter-study reproducibility was assessed (MEH) by re-imaging seven subjects one to two days after the first scan. Inter-observer variability was assessed by a second observer, analyzing seven of the data sets (JMF). For the intra-observer variability, one observer (MEH) analyzed the first seven data sets and waited six weeks to re-analyze the same seven data sets."

3. Page 6, para 2: How did you decide on the specific parameter setting for the various imaging sequence permutations? Were they realistically modeled after the sequence parameters from other manufacturers?

Response:

The specific sequence parameter settings were duplicated from those used in previous published works. Specifically, refs Alfakih et al, Moon et al and Hudsmith et al.

The text now described the parameters used in the context of this previous work.

"After localization and piloting, a short-axis stack was acquired parallel to the atrioventricular groove to cover the entire left ventricle in the standard way [12,13] for the 7/3mm (TE/TR 1.5/3.0 ms, flip angle 60^{o}, temporal resolution 45ms, slices/breathold 1, matrix size 256 x 202, field of view 380 x 309 mm) identical to

those parameters described by Hudsmith et al[12] and consistent with the parameters used by Moon et al [3], 7/0mm (TE/TR 1.5/3.0 ms, flip angle 60^{o}, temporal resolution 45ms, slices/breath-hold 1, matrix size 256 x 202, field of view 380 x 309 mm) as the above sequence but without the 3mm gaps, and 6/4mm sequences (TE/TR 1.7/3.4 ms, flip angle 55^{o}, temporal resolution 42ms, slices/breath-hold 2, matrix size 192 x 192, field of view 360 x 292 mm) duplicating that of the parameters described by Alfakih et al[1]. "

4. Page 7, para 2: How was the analysis blinded? Was all information pertaining to patients and imaging parameters removed from the images?

Response:

This is correct. The usual information regarding sequence parameters and patient details were removed by a person not involved in the analysis.

5. Page 8, para 1: "The inter-study reproducibility was assessed by re-imaging seven subjects." At what interval? If during the same imaging session, were patients taken off the table, ECG leads taken off and re-applied?

Response:

To study true inter-study reproducibility we re-imaged the subjects within 1-2 days of the first study. New positioning on the table, new ECG lead positioning, re-piloting the heart for acquisition of the short axis stack of cine images were therefore contributing to the inter-study variability. This is therefore true interstudy reproducibility rather than just re-imaging in the same position a few minutes after the first scan. We have therefore added this missing information to the revised manuscript: "The inter-study reproducibility was assessed by re-imaging seven subjects one to two days after the first scan."

Finally, please, add one or more references on the same or similar subject from earlier issues of the Int J Cardiovascular Imaging

Response:

We have added two more references from earlier issues of the Int J Cardiovascular Imaging as requested. Darasz et al and Mao et al. We did not consider any of the other publications appropriate for inclusion in the reference list.

Effects of Steady State Free Precession Parameters on Cardiac Mass, Function, and Volumes

Short title: Effects of SSFP parameters on cardiac volume studies

Maureen C. Hogan, MD, MSc, BSc, Steffen E. Petersen, MD, DPhil, Lucy E. Hudsmith, MA, MRCP, Jane M. Francis, DCCR, DNM, Stefan Neubauer, MD, FRCP & Matthew D. Robson, PhD

From the University of Oxford Centre for Clinical Magnetic Resonance Research, Department of Cardiovascular Medicine, University of Oxford, John Radcliffe Hospital, Oxford, UK

Word count: 3387

Address for correspondence:

Matthew D. Robson, PhD
University of Oxford Centre for Clinical Magnetic Resonance Research
Department of Cardiovascular Medicine
John Radcliffe Hospital
Oxford
OX3 9DU
Phone: +44 1865 857670
Fax: +44 1865 221111
E-mail: matthew.robson@cardiov.ox.ac.uk

This study was supported by grants from the British Heart Foundation (SEP, LEH, SN), the Medical Research Council (MDR), the Wellcome Trust (SN) and the Rhodes Scholarship (MCH).

Key words: Interslice gap; Magnetic resonance imaging; Slice thickness; Temporal resolution; Ventricular function

ABSTRACT

Purpose. We aimed to investigate comparability of LV volumes, function, and mass acquired with three steady-state free precession (SSFP) pulse sequences, simulating typical vendor and protocol specific differences in data acquisition.

Methods. Twenty-one healthy subjects (11 male and 10 female; age range 23-49) underwent cardiac magnetic resonance (CMR) imaging at 1.5 Tesla (T). A complete stack of short-axis views covering the entire left ventricle (LV) were acquired for each of the three SSFP sequences, differing in the interslice gap and slice thickness (7mm with no gap (7/0mm); 7mm with a 3mm gap (7/3mm) and 6mm with a 4mm gap (6/4mm)) with slight variations in acquisition parameters. For each sequence, the LV volumes, function, and mass were determined. Intra- and inter-observer variability and inter-study reproducibility were assessed for all protocols.

Results. All LV volumes, function and mass parameters were similar for the three SSFP sequences ($p>0.05$ for all). The LV ejection fraction for the 7/3 mm sequence was 67.2 ± 6.0, 67.4 ± 5.3 for the 7/0mm sequence, and the 6/4 mm sequence was 69.2 ± 5.7. The LV mass ranged from 119.8 ± 32.4 for the 7/3 mm sequence to 122.2 ± 34.0 for the 7/0 mm sequence. Variabilities were low with no difference in variability between the sequences.

Conclusion. The three SSFP pulse sequence techniques resulted in similar LV volume, function, and mass measurements with no difference in observer and interstudy variabilities. This may allow application and transfer of LV volume studies and databases

based on different imaging parameters, at different CMR sites, with a given post-processing method. Future multi-centre studies may now be in a position to consider multi-vendor study designs for LV volume studies.

Abbreviations: ANOVA-analysis of variance; CMR-Cardiovascular magnetic resonance; CoV-Coefficient of variability; FISP- Fast imaging with steady state precession; FLASH-Fast low angle shot; Magnetic resonance imaging (MRI); T-Tesla; TE-Echo time; TR-Repetition time; LV-Left ventricle; SD-Standard deviation; SSFP-Steady-state free precession.

INTRODUCTION

Cardiovascular magnetic resonance (CMR) imaging is accurate and reproducible in measuring left ventricular (LV) volumes[1-3]. Evaluation of cardiac function parameters is necessary to diagnose heart disease and monitor ventricular function[4]. To diagnose, assess prognosis, and evaluate a patient's response to therapy, cardiac function parameters must be both accurate and reproducible [5-7].

The steady-state free precession (SSFP) pulse sequence at 1.5 Tesla (T) has been accepted as the preferred acquisition technique for cardiac functional assessment because it provides high-quality images with improved border definition compared to gradient echo sequences, such as the fast low angle shot sequence (FLASH) [3]. SSFP is the sequence of choice for analysis of ventricular function because of the excellent endocardial contour contrast, resulting from the contrast between the ventricular blood and myocardium and between the myocardium and epicardial fat [8]. Further, this pulse sequence has been validated in animal models [9,10].

Different manufacturers of CMR machines alter subtle aspects of the SSFP acquisition parameters, such as resolution, flip angle, slice thickness, and interslice gap. From a clinical perspective, it is critically important that results obtained from different CMR machines and from various manufacturers are interchangeable as even small differences in cardiac parameters can influence patient treatment,e.g Implantable cardioverter defibrillator indications are partly based on cut-off values for ejection fraction of less than 30 or 35%. . Various groups have determined cardiac parameters using SSFP for

normal populations [1,11,12]. Although all these sequences are described as SSFP, it is unclear whether the cardiac volume, function, and mass measurements are comparable with different acquisition parameters. Moon and colleagues [3] have previously demonstrated that different sequences, FLASH and SSFP, result in significantly different left ventricular volumes and masses. Different parameter selection and slice thickness within the SSFP sequence may also influence cardiac parameters. To date, no study has compared variations within the SSFP pulse sequence technique.

The accuracy and reproducibility of breathhold CMR in analyzing cardiac volumes, function, and mass in heart failure compared to echocardiography allows for a reduction in the number of patients needed to prove a hypothesis in clinical trials [5]. We propose that if SSFP pulse sequence techniques are interchangeable from site-to-site, then multi-center trials will benefit because CMR will allow for combining patients from different sites.

The purpose of this study was to compare three SSFP pulse sequence techniques with slight variations in slice thickness and interslice gap, flip angle, repetition time (TR), echo time (TE), matrix size, and field of view, to determine if the techniques are comparable and therefore interchangeable. We hypothesized there would not be a significant difference among the three SSFP pulse sequence techniques**.**

METHODS

Study Population

Twenty-one healthy subjects with a mean age of 30 ± 7 years (11 males, 10 females) were investigated. All subjects were non-smokers with no family history of coronary artery disease and a normal resting electrocardiogram. The mean blood pressure was (123 ± 15)/ (77 ± 10 mmHg), heart rate was 63 ± 11 bpm, the mean weight was 72 ± 13 kg with a mean body mass index of 24 ± 3 kg/m^2 and mean body surface area was 1.86 ± 0.19 m^2. Subjects with typical contraindications to magnetic resonance imaging (MRI), such as claustrophobia or pacemakers, were excluded. The study was carried out according to the principles of the Declaration of Helsinki and was approved by our institutional ethics committee. Each volunteer gave informed written consent.

Magnetic Resonance Imaging Protocol

All subjects were examined on a 1.5T Siemens Sonata imager (Siemens Medical Solutions, Erlangen, Germany) with Syngo software Version 21B, equipped with high performance gradients (40mT/m peak, 200T/m/s slew-rate), prospective electrocardiographic gating and the subject in the supine position. A standard six-channel anterior cardiac array and two-elements of the integrated spine array coil were used. Three experienced operators performed the scans (LEH, SEP, JMF). After localization and piloting, a short-axis stack was acquired parallel to the atrioventricular groove to cover the entire left ventricle in the standard way [12,13] for the 7/3mm (TE/TR 1.5/3.0 ms, flip angle 60^o, temporal resolution 45ms, slices/breathold 1, matrix size 256 x 202,

field of view 380 x 309 mm) identical to those parameters described by Hudsmith et al[12] and consistent with the parameters used by Moon et al [3], 7/0mm (TE/TR 1.5/3.0 ms, flip angle 60^{o}, temporal resolution 45ms, slices/breath-hold 1, matrix size 256 x 202, field of view 380 x 309 mm) as the above sequence but without the 3mm gaps, and 6/4mm sequences (TE/TR 1.7/3.4 ms, flip angle 55^{o}, temporal resolution 42ms, slices/breath-hold 2, matrix size 192 x 192, field of view 360 x 292 mm) duplicating that of the parameters described by Alfakih et al[1]. All images were acquired during breath-hold in end-expiration. The total examination time was approximately 40 minutes for each subject.

Image Analysis

Blinded analysis was performed using Argus software (Version 2002B, Siemens Medical Solutions, Erlangen, Germany). The end-systolic and end-diastolic frames were independently chosen by each observer. Using the standard format [12,13] on each end-diastolic frame, endocardial and epicardial borders were manually traced, and an endocardial border was manually traced on each end-systolic frame . The end-diastolic frame was defined as the image with the largest ventricular volume in each series, and the image with the smallest ventricular volume was chosen as the end-systolic frame. The interventricular septum was included as a part of the left ventricle. From these data, the ejection fraction, LV end-diastolic volume, LV end-systolic volume, stroke volume, and LV mass were calculated. Myocardial mass was calculated by multiplication of the tissue volume by 1.05 g/cm^3 (specific density of myocardium).

Reproducibility and Variability

The inter-study reproducibility was assessed (MEH) by re-imaging seven subjects one to two days after the first scan. Inter-observer variability was assessed by a second observer, analyzing seven of the data sets (JMF). For the intra-observer variability, one observer (MEH) analyzed the first seven data sets and waited six weeks to re-analyze the same seven data sets.

Statistical Analysis

All data are presented as mean +/- standard deviation (SD) unless stated otherwise. Inter-study reproducibility, inter- and intra-observer variability were assessed using the method of Bland and Altman [14]. The coefficient of variability (CoV) was calculated as the SD of the differences between the two sets of measurements divided by the mean value of the parameter under consideration. Repeated measures of analysis of variance (ANOVA) were used to test for differences for continuous parameters among the three sequences used. Throughout the analyses, a two-sided p-value of <0.05 was considered statistically significant. All computations were performed with SPSS 11.5 (SPSS Inc., Chicago, US). Sample size calculations were performed before the initiation of the study based on the following assumptions: repeated measures ANOVA, SD for LV mass in healthy population [1], power 90%, alpha 0.05 and a difference of 10% of LV mass as the change to be detected.

RESULTS

CMR imaging was well tolerated by all subjects. All datasets were of good image quality and included in the study. Images acquired of a healthy female subject using the three SSFP pulse sequence techniques are shown in Figure 1.

The LV volumes, function and mass for each sequence are displayed in Table 1. There was no significant difference in all LV parameters using the three acquisition techniques ($p>0.05$), with similar normal ranges for healthy volunteers. There was a trend for sequence 6/4mm to have an increased LV ejection fraction ($p=0.07$) and a reduced end-systolic volume ($p=0.05$).

There was no systematic difference in variabilities for the three sequences (Table 2). The LV ejection fraction and LV mass for the intraobserver variability are displayed in Figure 2. The intraobserver variability was lowest using the 6/4mm technique for the LV ejection fraction, LV end-diastolic volume, and LV mass. For the LV ejection fraction, the interobserver variability was lowest for the 7/3 mm technique, and highest for the 6/4mm technique.

DISCUSSION

The purpose of this study was to quantify LV volumes, function and mass using three SSFP pulse sequence techniques to assess if the techniques are comparable and therefore interchangeable. We have shown that the three pulse sequences result in no significant differences in left ventricular volumes, function, and mass. Our results for the 6/4mm technique were comparable to the normal range of cardiac parameters published by Alfakih et al, using a Philips 1.5 T SSFP sequence using a 6 mm slice and 4 mm gap[1]. The normal range published by Hudsmith et al using a Siemens 1.5 T SSFP sequence with a 7 mm slice and 3 mm gap showed cardiac parameters similar to our 7/3mm technique[12]. Kunz et al [8] examined left ventricular parameters using a contiguous 8/0mm technique using a Siemens 1.5T SSFP sequence, showing results similar to our 7/0mm contiguous technique.

There was no significant difference in LV mass for all three sequences. The 6/4mm technique showed a trend towards a decreased end-systolic volume. This is possibly due to the larger interslice gap, leading to more geometric assumptions. The 6/4mm technique had a trend towards an increased ejection fraction. The 6/4mm technique had a higher temporal resolution (i.e. lower TR) than the other two techniques, and therefore the captured end-systolic frame may be closer to the true end-systole, resulting in higher ejection fractions when compared to the two other sequences with lower temporal resolution. The lower spatial resolution of the 6/4 mm technique (1.9 x 1.5 mm) compared to the other two techniques (1.5 x 1.5 mm) may also contribute to the observed trend for differences in LV end-systolic volume and ejection fraction.

One would assume that although the 7/0mm technique has the longest acquisition time, it would be clinically superior to the other techniques because images are acquired contiguously, covering the entire ventricle, thus eliminating any gaps and not relying on geometric assumptions. However, this study has shown that patient examination time can be minimized by using technique 7/3mm and 6/4mm, and result in similar and interchangeable cardiac parameter measurement. The application of these two techniques are therefore valuable in a time-pressured clinical environment.

The variability measurements of this study are comparable with those reported in the literature [1,3,11-13]. Overall, our results show low variability for all LV volumes, function, and mass results. These variability data show that the tested techniques are reproducible and can be used in clinical practice.

The LV ejection fraction is a frequently used cardiac functional prognostic factor for patients, particularly in monitoring responses to therapeutic intervention [15] . We have shown these three techniques provide the same information regardless of the manufacturer. This is important for patients receiving care in different geographical locations or within a multi-centre trial. We have provided evidence that may allow application and transfer of LV volume databases based on slightly different SSFP parameters, slice thickness and inter-slice gaps at different MRI sites, given a similar approach to post-processing. Future multi-centre studies may now be in a position to consider multi-vendor study designs for LV volume studies, aiding recruitment.

It is probable that variability in cardiac parameters result from variations in operators. Intra- and inter-operator variability studies of manual planning of CMR imaging resulted in insignificant statistical differences on LV parameters [16]. Because the variations due to different operators are insignificant, it was important to analyze if the errors were the result of the difference in the manufacturer, as completed in our study.

CONCLUSION

We have shown the LV volume, function, and mass parameters acquired at 1.5T using three SSFP pulse sequence techniques in healthy controls are comparable and interchangeable. This finding is particularly important for patients receiving care in different geographical locations and may allow multi-centre trials to include multiple vendor CMR centers, optimizing patient recruitment. However, future studies may need to confirm our findings in patients with dilated or hypertrophied hearts.

FIGURE LEGEND

Figure 1: Mid-ventricular short axis slices acquired during end-diastole in a healthy female subject using three steady-state free precession pulse sequence techniques, with endocardial and epicardial contours drawn on the left ventricle. A: 7 mm slice thickness with a 3 mm gap, one slice per breath-hold. B: contiguous images acquired with no gap at 7mm, one slice per breath-hold. C: 6 mm slice thickness with a 4 mm gap, two slices per breath-hold.

Figure 2: Intraobserver variability for LV mass and LV ejection fraction using the steady state free precession sequence without interslice gap for 7 healthy subjects (Bland-Altman plot [14]).

REFERENCES

1. Alfakih K, Plein S, Thiele H, Jones T, Ridgway JP, Sivananthan MU. Normal human left and right ventricular dimensions for MRI as assessed by turbo gradient echo and steady-state free precession imaging sequences. J Magn Reson Imaging 2003;17:323-329.
2. Grothues F, Smith GC, Moon JC, Bellenger NG, Collins P, Klein HU, et al. Comparison of interstudy reproducibility of cardiovascular magnetic resonance with two-dimensional echocardiography in normal subjects and in patients with heart failure or left ventricular hypertrophy. Am J Cardiol 2002;90:29-34.
3. Moon JC, Lorenz CH, Francis JM, Smith GC, Pennell DJ. Breath-hold FLASH and FISP cardiovascular MR imaging: left ventricular volume differences and reproducibility. Radiology 2002;223:789-797.
4. Di Cesare E, Catalucci A, Masciocchi C. Left ventricular function: MRI assessment. Rays 1999;24:19-32.
5. Bellenger NG, Davies LC, Francis JM, Coats AJ, Pennell DJ. Reduction in sample size for studies of remodeling in heart failure by the use of cardiovascular magnetic resonance. J Cardiovasc Magn Reson 2000;2:271-278.
6. Darasz KH, Underwood SR, Bayliss J, Forbat SM, Keegan J, Poole-Wilson PA, et al. Measurement of left ventricular volume after anterior myocardial infarction: comparison of magnetic resonance imaging, echocardiography, and radionuclide ventriculography. Int J Cardiovasc Imaging 2002;18:135-142.
7. Mao S, Takasu J, Child J, Carson S, Oudiz R, Budoff MJ. Comparison of LV mass and volume measurements derived from electron beam tomography using cine imaging and angiographic imaging. Int J Cardiovasc Imaging 2003;19:439-445.
8. Kunz RP, Oellig F, Krummenauer F, Oberholzer K, Romaneehsen B, Vomweg TW, et al. Assessment of left ventricular function by breath-hold cine MR imaging: Comparison of different steady-state free precession sequences. J Magn Reson Imaging 2005;21:140-148.
9. Fieno DS, Jaffe WC, Simonetti OP, Judd RM, Finn JP. TrueFISP: assessment of accuracy for measurement of left ventricular mass in an animal model. J Magn Reson Imaging 2002;15:526-531.
10. Shors SM, Fung CW, Francois CJ, Finn JP, Fieno DS. Accurate quantification of right ventricular mass at MR imaging by using cine true fast imaging with steady-state precession: study in dogs. Radiology 2004;230:383-388.
11. Sandstede J, Lipke C, Beer M, Hofmann S, Pabst T, Kenn W, et al. Age- and gender-specific differences in left and right ventricular cardiac function and mass determined by cine magnetic resonance imaging. Eur Radiol 2000;10:438-442.
12. Hudsmith LE, Petersen SE, Francis JM, Robson MD, Neubauer S. Normal human left and right ventricular and left atrial dimensions using steady state free precession magnetic resonance imaging. J Cardiovasc Magn Reson 2005;7:775-782.

13. Lorenz CH, Walker ES, Morgan VL, Klein SS, Graham TP, Jr. Normal human right and left ventricular mass, systolic function, and gender differences by cine magnetic resonance imaging. J Cardiovasc Magn Reson 1999;1:7-21.
14. Bland JM, Altman DG. Statistical methods for assessing agreement between two methods of clinical measurement. Lancet 1986;1:307-310.
15. Selvanayagam J, Westaby S, Channon K, Francis J, Eichhofer J, Saito S, et al. Images in cardiovascular medicine. Surgical left ventricular restoration: an extreme case. Circulation 2003;107:e71.
16. Danilouchkine MG, Westenberg JJ, de Roos A, Reiber JH, Lelieveldt BP. Operator induced variability in cardiovascular MR: left ventricular measurements and their reproducibility. J Cardiovasc Magn Reson 2005;7:447-457.

Table 1: LV measurements in 21 healthy subjects

	7/3mm	7/0mm	6/4mm	P value
Ejection fraction (%)	67.2 ± 6.0 (64.5-70.0)	67.4 ± 5.3 (65.0-69.8)	69.2 ± 5.7 (66.6-71.8)	0.07
Mass (g)	119.8 ± 32.4 (105.1-134.5)	122.2 ± 34.0 (106.6-137.7)	119.8 ± 33.6 (104.5-135.1)	0.35
End-diastolic volume (ml)	155.8 ± 34.0 (140.3-171.2)	159.7 ± 36.3 (143.2-176.2)	157.8 ± 34.7 (142.1-173.6)	0.10
End-systolic volume (ml)	50.6 ± 12.9 (44.8-56.5)	52.3 ± 16.0 (45.0-59.6)	48.2 ± 12.3 (42.6-53.8)	0.05
Stroke volume (ml)	105.1 ± 27.0 (92.8-117.4)	107.4 ± 24.4 (96.3-118.5)	109.7 ± 27.5 (97.2-122.2)	0.14

Values are expressed as Mean ± SD (95% confidence interval); ANOVA was used to test for differences for continuous parameters among the three sequences; $p<0.05$ is statistically significant.

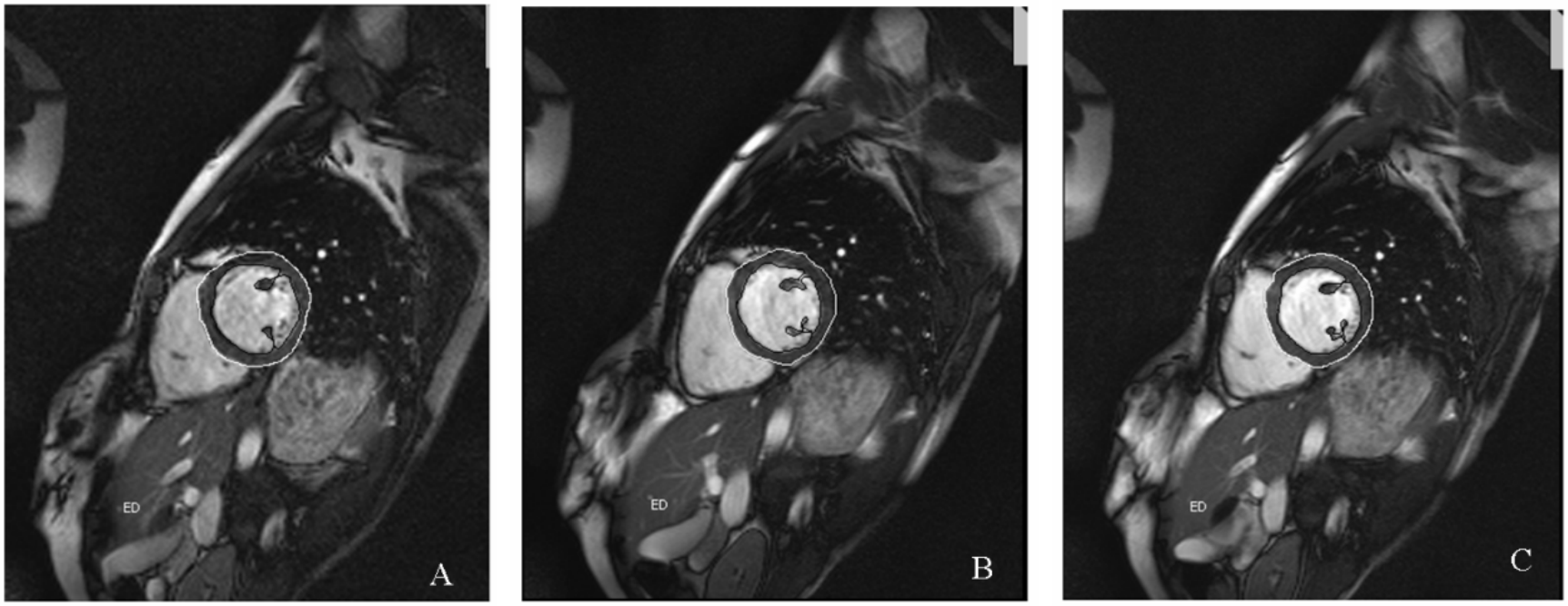
Table 2: Variability of left ventricular measurements

	Intraobserver		Interobserver		Interstudy	
	Bias (95% limits of agreement)	**CoV**	**Bias (95% limits of agreement)**	**CoV**	**Bias (95% limits of agreement)**	**CoV**
Ejection Fraction (%) 7/3mm	1.36 ± 3.43 (-5.36-8.08)	5.3	-2.75 ± 1.78 (-6.24-0.75)	2.8	2.06 ± 4.97 (-7.67-11.80)	7.8
Ejection Fraction (%) 7/0mm	3.14 ± 5.78 (-8.19-14.47)	9.1	-1.54 ± 2.91 (-7.24-4.15)	4.6	2.36 ± 5.40 (-8.22-12.95)	8.4
Ejection Fraction (%) 6/4mm	0.43 ± 2.49 (-4.45-5.31)	3.7	-1.19 ± 4.67 (-10.35-7.97)	7.2	2.47 ± 4.48 (-6.32-11.26)	6.8
Mass (g) 7/3mm	4.26 ± 6.67 (-8.80-17.33)	5.6	5.63 ± 10.28 (-14.51-25.77)	9.0	4.71 ± 12.21 (-19.23-28.65)	10.3
Mass (g) 7/0mm	1.67 ± 6.94 (-11.93-15.27)	5.8	9.07 ± 7.53 (-5.69-23.82)	6.5	-0.74 ± 10.72 (-21.75-20.26)	8.9
Mass (g) 6/4mm	4.18 ± 4.95 (-5.51-13.88)	4.2	4.93 ± 9.54 (-13.77-23.63)	8.3	2.21 ± 14.85 (-26.90-31.32)	12.5
End-diastolic volume (ml) 7/3mm	-6.61 ± 9.14 (-24.52 – 11.30)	6.9	10.17 ± 6.57 (-2.70-23.04)	4.6	-0.73 ± 12.62 (-25.48 – 24.01)	8.5
End-diastolic volume (ml) 7/0mm	-6.45 ± 8.15 (-22.42 – 9.53)	5.3	13.17 ± 8.13 (-2.77-29.10)	5.6	-1.97 ± 14.22 (-29.83 – 25.89)	9.5
End-diastolic volume (ml) 6/4mm	-5.73 ± 7.56 (-20.54 - 9.09)	5.0	13.09 ± 15.05 (-16.41-42.59)	10.6	0.10 ± 18.98 (-37.10 – 37.29)	12.8

Values are expressed as Mean ± SD (95% confidence interval); CoV= coefficient of variability; Mean and confidence interval determined according to the Bland and Altman method [14].

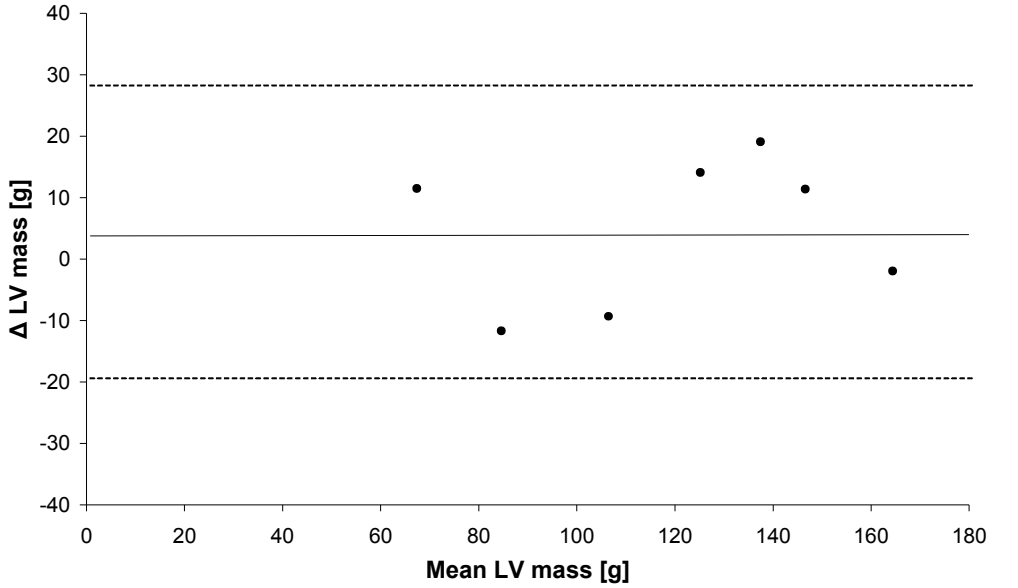
line figure

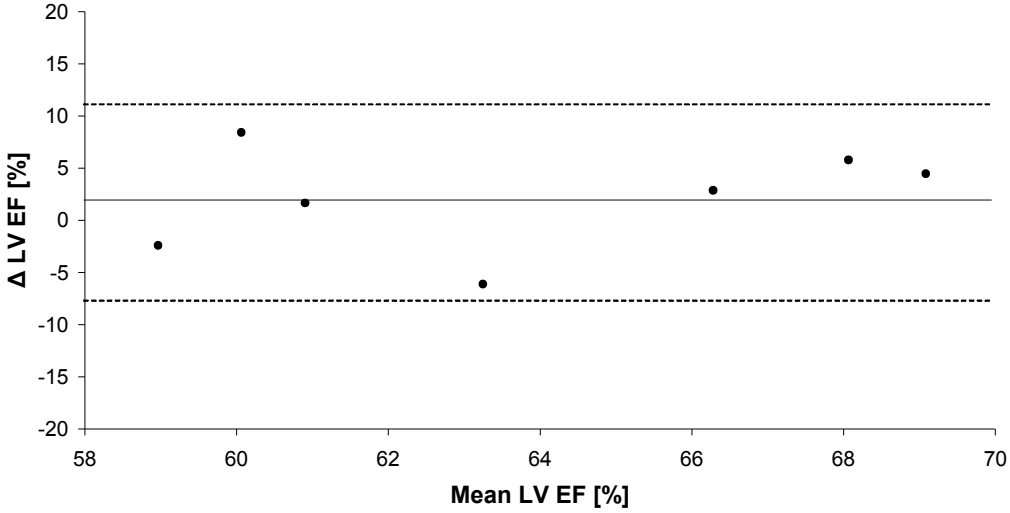
Click here to download line figure: Hogan_effects of SSFP_31May2006_figure 1.ppt



line figure

Click here to download line figure: Hogan_effects of SSFP_31May2006_figure 2.ppt





Effects of Steady State Free Precession Parameters on Cardiac Mass, Function, and Volumes

Short title: Effects of SSFP parameters on cardiac volume studies

Maureen C. Hogan, MD, MSc, BSc, Steffen E. Petersen, MD, DPhil, Lucy E. Hudsmith, MA, MRCP, Jane M. Francis, DCCR, DNM, Stefan Neubauer, MD, FRCP & Matthew D. Robson, PhD

From the University of Oxford Centre for Clinical Magnetic Resonance Research, Department of Cardiovascular Medicine, University of Oxford, John Radcliffe Hospital, Oxford, UK

Word count: 3387

Address for correspondence:

Matthew D. Robson, PhD
University of Oxford Centre for Clinical Magnetic Resonance Research
Department of Cardiovascular Medicine
John Radcliffe Hospital
Oxford
OX3 9DU
Phone: +44 1865 857670
Fax: +44 1865 221111
E-mail: matthew.robson@cardiov.ox.ac.uk

This study was supported by grants from the British Heart Foundation (SEP, LEH, SN), the Medical Research Council (MDR), the Wellcome Trust (SN) and the Rhodes Scholarship (MCH).

Key words: Interslice gap; Magnetic resonance imaging; Slice thickness; Temporal resolution; Ventricular function

ABSTRACT

Purpose. We aimed to investigate comparability of LV volumes, function, and mass acquired with three steady-state free precession (SSFP) pulse sequences, simulating typical vendor and protocol specific differences in data acquisition.

Methods. Twenty-one healthy subjects (11 male and 10 female; age range 23-49) underwent cardiac magnetic resonance (CMR) imaging at 1.5 Tesla (T). A complete stack of short-axis views covering the entire left ventricle (LV) were acquired for each of the three SSFP sequences, differing in the interslice gap and slice thickness (7mm with no gap (7/0mm); 7mm with a 3mm gap (7/3mm) and 6mm with a 4mm gap (6/4mm)) with slight variations in acquisition parameters. For each sequence, the LV volumes, function, and mass were determined. Intra- and inter-observer variability and inter-study reproducibility were assessed for all protocols.

Results. All LV volumes, function and mass parameters were similar for the three SSFP sequences ($p>0.05$ for all). The LV ejection fraction for the 7/3 mm sequence was 67.2 ± 6.0, 67.4 ± 5.3 for the 7/0mm sequence, and the 6/4 mm sequence was 69.2 ± 5.7. The LV mass ranged from 119.8 ± 32.4 for the 7/3 mm sequence to 122.2 ± 34.0 for the 7/0 mm sequence. Variabilities were low with no difference in variability between the sequences.

Conclusion. The three SSFP pulse sequence techniques resulted in similar LV volume, function, and mass measurements with no difference in observer and interstudy variabilities. This may allow application and transfer of LV volume studies and databases

based on different imaging parameters, at different CMR sites, with a given post-processing method. Future multi-centre studies may now be in a position to consider multi-vendor study designs for LV volume studies.

Abbreviations: ANOVA-analysis of variance; CMR-Cardiovascular magnetic resonance; CoV-Coefficient of variability; FISP- Fast imaging with steady state precession; FLASH-Fast low angle shot; Magnetic resonance imaging (MRI); T-Tesla; TE-Echo time; TR-Repetition time; LV-Left ventricle; SD-Standard deviation; SSFP-Steady-state free precession.

INTRODUCTION

Cardiovascular magnetic resonance (CMR) imaging is accurate and reproducible in measuring left ventricular (LV) volumes[1-3]. Evaluation of cardiac function parameters is necessary to diagnose heart disease and monitor ventricular function[4]. To diagnose, assess prognosis, and evaluate a patient's response to therapy, cardiac function parameters must be both accurate and reproducible [5-7].

The steady-state free precession (SSFP) pulse sequence at 1.5 Tesla (T) has been accepted as the preferred acquisition technique for cardiac functional assessment because it provides high-quality images with improved border definition compared to gradient echo sequences, such as the fast low angle shot sequence (FLASH) [3]. SSFP is the sequence of choice for analysis of ventricular function because of the excellent endocardial contour contrast, resulting from the contrast between the ventricular blood and myocardium and between the myocardium and epicardial fat [8]. Further, this pulse sequence has been validated in animal models [9,10].

Different manufacturers of CMR machines alter subtle aspects of the SSFP acquisition parameters, such as resolution, flip angle, slice thickness, and interslice gap. From a clinical perspective, it is critically important that results obtained from different CMR machines and from various manufacturers are interchangeable as even small differences in cardiac parameters can influence patient treatment, e.g Implantable cardioverter defibrillator indications are partly based on cut-off values for ejection fraction of less than 30 or 35%. . Various groups have determined cardiac parameters using SSFP for

Deleted: and prognosis

normal populations [1,11,12]. Although all these sequences are described as SSFP, it is unclear whether the cardiac volume, function, and mass measurements are comparable with different acquisition parameters. Moon and colleagues [3] have previously demonstrated that different sequences, FLASH and SSFP, result in significantly different left ventricular volumes and masses. Different parameter selection and slice thickness within the SSFP sequence may also influence cardiac parameters. To date, no study has compared variations within the SSFP pulse sequence technique.

The accuracy and reproducibility of breathhold CMR in analyzing cardiac volumes, function, and mass in heart failure compared to echocardiography allows for a reduction in the number of patients needed to prove a hypothesis in clinical trials [5]. We propose that if SSFP pulse sequence techniques are interchangeable from site-to-site, then multi-center trials will benefit because CMR will allow for combining patients from different sites.

The purpose of this study was to compare three SSFP pulse sequence techniques with slight variations in slice thickness and interslice gap, flip angle, repetition time (TR), echo time (TE), matrix size, and field of view, to determine if the techniques are comparable and therefore interchangeable. We hypothesized there would not be a significant difference among the three SSFP pulse sequence techniques.

METHODS

Study Population

Twenty-one healthy subjects with a mean age of 30 ± 7 years (11 males, 10 females) were investigated. All subjects were non-smokers with no family history of coronary artery disease and a normal resting electrocardiogram. The mean blood pressure was (123 ± 15)/ (77 ± 10 mmHg), heart rate was 63 ± 11 bpm, the mean weight was 72 ± 13 kg with a mean body mass index of 24 ± 3 kg/m^2 and mean body surface area was 1.86 ± 0.19 m^2. Subjects with typical contraindications to magnetic resonance imaging (MRI), such as claustrophobia or pacemakers, were excluded. The study was carried out according to the principles of the Declaration of Helsinki and was approved by our institutional ethics committee. Each volunteer gave informed written consent.

Magnetic Resonance Imaging Protocol

All subjects were examined on a 1.5T Siemens Sonata imager (Siemens Medical Solutions, Erlangen, Germany) with Syngo software Version 21B, equipped with high performance gradients (40mT/m peak, 200T/m/s slew-rate), prospective electrocardiographic gating and the subject in the supine position. A standard six-channel anterior cardiac array and two-elements of the integrated spine array coil were used. Three experienced operators performed the scans (LEH, SEP, JMF). After localization and piloting, a short-axis stack was acquired parallel to the atrioventricular groove to cover the entire left ventricle in the standard way [12,13] for the 7/3mm (TE/TR 1.5/3.0 ms, flip angle 60^o, temporal resolution 45ms, slices/breathold 1, matrix size 256 x 202,

field of view 380 x 309 mm) identical to those parameters described by Hudsmith et al[12] and consistent with the parameters used by Moon et al [3], 7/0mm (TE/TR 1.5/3.0 ms, flip angle 60^{o}, temporal resolution 45ms, slices/breath-hold 1, matrix size 256 x 202, field of view 380 x 309 mm) as the above sequence but without the 3mm gaps, and 6/4mm sequences (TE/TR 1.7/3.4 ms, flip angle 55^{o}, temporal resolution 42ms, slices/breath-hold 2, matrix size 192 x 192, field of view 360 x 292 mm) duplicating that of the parameters described by Alfakih et al[1]. All images were acquired during breath-hold in end-expiration. The total examination time was approximately 40 minutes for each subject.

Image Analysis

Blinded analysis was performed using Argus software (Version 2002B, Siemens Medical Solutions, Erlangen, Germany). The end-systolic and end-diastolic frames were independently chosen by each observer. Using the standard format [12,13] on each end-diastolic frame, endocardial and epicardial borders were manually traced, and an endocardial border was manually traced on each end-systolic frame . The end-diastolic frame was defined as the image with the largest ventricular volume in each series, and the image with the smallest ventricular volume was chosen as the end-systolic frame. The interventricular septum was included as a part of the left ventricle. From these data, the ejection fraction, LV end-diastolic volume, LV end-systolic volume, stroke volume, and LV mass were calculated. Myocardial mass was calculated by multiplication of the tissue volume by 1.05 g/cm^{3} (specific density of myocardium).

Reproducibility and Variability

The inter-study reproducibility was assessed (MEH) by re-imaging seven subjects one to two days after the first scan. Inter-observer variability was assessed by a second observer, analyzing seven of the data sets (JMF). For the intra-observer variability, one observer (MEH) analyzed the first seven data sets and waited six weeks to re-analyze the same seven data sets.

Deleted:

Statistical Analysis

All data are presented as mean +/- standard deviation (SD) unless stated otherwise. Inter-study reproducibility, inter- and intra-observer variability were assessed using the method of Bland and Altman [14]. The coefficient of variability (CoV) was calculated as the SD of the differences between the two sets of measurements divided by the mean value of the parameter under consideration. Repeated measures of analysis of variance (ANOVA) were used to test for differences for continuous parameters among the three sequences used. Throughout the analyses, a two-sided p-value of <0.05 was considered statistically significant. All computations were performed with SPSS 11.5 (SPSS Inc., Chicago, US). Sample size calculations were performed before the initiation of the study based on the following assumptions: repeated measures ANOVA, SD for LV mass in healthy population [1], power 90%, alpha 0.05 and a difference of 10% of LV mass as the change to be detected.

RESULTS

CMR imaging was well tolerated by all subjects. All datasets were of good image quality and included in the study. Images acquired of a healthy female subject using the three SSFP pulse sequence techniques are shown in Figure 1.

The LV volumes, function and mass for each sequence are displayed in Table 1. There was no significant difference in all LV parameters using the three acquisition techniques ($p>0.05$), with similar normal ranges for healthy volunteers. There was a trend for sequence 6/4mm to have an increased LV ejection fraction ($p=0.07$) and a reduced end-systolic volume ($p=0.05$).

There was no systematic difference in variabilities for the three sequences (Table 2). The LV ejection fraction and LV mass for the intraobserver variability are displayed in Figure 2. The intraobserver variability was lowest using the 6/4mm technique for the LV ejection fraction, LV end-diastolic volume, and LV mass. For the LV ejection fraction, the interobserver variability was lowest for the 7/3 mm technique, and highest for the 6/4mm technique.

DISCUSSION

The purpose of this study was to quantify LV volumes, function and mass using three SSFP pulse sequence techniques to assess if the techniques are comparable and therefore interchangeable. We have shown that the three pulse sequences result in no significant differences in left ventricular volumes, function, and mass. Our results for the 6/4mm technique were comparable to the normal range of cardiac parameters published by Alfakih et al, using a Philips 1.5 T SSFP sequence using a 6 mm slice and 4 mm gap[1]. The normal range published by Hudsmith et al using a Siemens 1.5 T SSFP sequence with a 7 mm slice and 3 mm gap showed cardiac parameters similar to our 7/3mm technique[12]. Kunz et al [8] examined left ventricular parameters using a contiguous 8/0mm technique using a Siemens 1.5T SSFP sequence, showing results similar to our 7/0mm contiguous technique.

There was no significant difference in LV mass for all three sequences. The 6/4mm technique showed a trend towards a decreased end-systolic volume. This is possibly due to the larger interslice gap, leading to more geometric assumptions. The 6/4mm technique had a trend towards an increased ejection fraction. The 6/4mm technique had a higher temporal resolution (i.e. lower TR) than the other two techniques, and therefore the captured end-systolic frame may be closer to the true end-systole, resulting in higher ejection fractions when compared to the two other sequences with lower temporal resolution. The lower spatial resolution of the 6/4 mm technique (1.9 x 1.5 mm) compared to the other two techniques (1.5 x 1.5 mm) may also contribute to the observed trend for differences in LV end-systolic volume and ejection fraction.

Deleted:

Deleted:

Deleted:

One would assume that although the 7/0mm technique has the longest acquisition time, it would be clinically superior to the other techniques because images are acquired contiguously, covering the entire ventricle, thus eliminating any gaps and not relying on geometric assumptions. However, this study has shown that patient examination time can be minimized by using technique 7/3mm and 6/4mm, and result in similar and interchangeable cardiac parameter measurement. The application of these two techniques are therefore valuable in a time-pressured clinical environment.

The variability measurements of this study are comparable with those reported in the literature [1,3,11-13]. Overall, our results show low variability for all LV volumes, function, and mass results. These variability data show that the tested techniques are reproducible and can be used in clinical practice.

The LV ejection fraction is a frequently used cardiac functional prognostic factor for patients, particularly in monitoring responses to therapeutic intervention [15] . We have shown these three techniques provide the same information regardless of the manufacturer. This is important for patients receiving care in different geographical locations or within a multi-centre trial. We have provided evidence that may allow application and transfer of LV volume databases based on slightly different SSFP parameters, slice thickness and inter-slice gaps at different MRI sites, given a similar approach to post-processing. Future multi-centre studies may now be in a position to consider multi-vendor study designs for LV volume studies, aiding recruitment.

It is probable that variability in cardiac parameters result from variations in operators. Intra- and inter-operator variability studies of manual planning of CMR imaging resulted in insignificant statistical differences on LV parameters [16]. Because the variations due to different operators are insignificant, it was important to analyze if the errors were the result of the difference in the manufacturer, as completed in our study.

CONCLUSION

We have shown the LV volume, function, and mass parameters acquired at 1.5T using three SSFP pulse sequence techniques in healthy controls are comparable and interchangeable. This finding is particularly important for patients receiving care in different geographical locations and may allow multi-centre trials to include multiple vendor CMR centers, optimizing patient recruitment. However, future studies may need to confirm our findings in patients with dilated or hypertrophied hearts.

FIGURE LEGEND

Figure 1: Mid-ventricular short axis slices acquired during end-diastole in a healthy female subject using three steady-state free precession pulse sequence techniques, with endocardial and epicardial contours drawn on the left ventricle. A: 7 mm slice thickness with a 3 mm gap, one slice per breath-hold. B: contiguous images acquired with no gap at 7mm, one slice per breath-hold. C: 6 mm slice thickness with a 4 mm gap, two slices per breath-hold.

Figure 2: Intraobserver variability for LV mass and LV ejection fraction using the steady state free precession sequence without interslice gap for 7 healthy subjects (Bland-Altman plot [14]).

REFERENCES

1. Alfakih K, Plein S, Thiele H, Jones T, Ridgway JP, Sivananthan MU. Normal human left and right ventricular dimensions for MRI as assessed by turbo gradient echo and steady-state free precession imaging sequences. J Magn Reson Imaging 2003;17:323-329.
2. Grothues F, Smith GC, Moon JC, Bellenger NG, Collins P, Klein HU, et al. Comparison of interstudy reproducibility of cardiovascular magnetic resonance with two-dimensional echocardiography in normal subjects and in patients with heart failure or left ventricular hypertrophy. Am J Cardiol 2002;90:29-34.
3. Moon JC, Lorenz CH, Francis JM, Smith GC, Pennell DJ. Breath-hold FLASH and FISP cardiovascular MR imaging: left ventricular volume differences and reproducibility. Radiology 2002;223:789-797.
4. Di Cesare E, Catalucci A, Masciocchi C. Left ventricular function: MRI assessment. Rays 1999;24:19-32.
5. Bellenger NG, Davies LC, Francis JM, Coats AJ, Pennell DJ. Reduction in sample size for studies of remodeling in heart failure by the use of cardiovascular magnetic resonance. J Cardiovasc Magn Reson 2000;2:271-278.
6. Darasz KH, Underwood SR, Bayliss J, Forbat SM, Keegan J, Poole-Wilson PA, et al. Measurement of left ventricular volume after anterior myocardial infarction: comparison of magnetic resonance imaging, echocardiography, and radionuclide ventriculography. Int J Cardiovasc Imaging 2002;18:135-142.
7. Mao S, Takasu J, Child J, Carson S, Oudiz R, Budoff MJ. Comparison of LV mass and volume measurements derived from electron beam tomography using cine imaging and angiographic imaging. Int J Cardiovasc Imaging 2003;19:439-445.
8. Kunz RP, Oellig F, Krummenauer F, Oberholzer K, Romaneehsen B, Vomweg TW, et al. Assessment of left ventricular function by breath-hold cine MR imaging: Comparison of different steady-state free precession sequences. J Magn Reson Imaging 2005;21:140-148.
9. Fieno DS, Jaffe WC, Simonetti OP, Judd RM, Finn JP. TrueFISP: assessment of accuracy for measurement of left ventricular mass in an animal model. J Magn Reson Imaging 2002;15:526-531.
10. Shors SM, Fung CW, Francois CJ, Finn JP, Fieno DS. Accurate quantification of right ventricular mass at MR imaging by using cine true fast imaging with steady-state precession: study in dogs. Radiology 2004;230:383-388.
11. Sandstede J, Lipke C, Beer M, Hofmann S, Pabst T, Kenn W, et al. Age- and gender-specific differences in left and right ventricular cardiac function and mass determined by cine magnetic resonance imaging. Eur Radiol 2000;10:438-442.
12. Hudsmith LE, Petersen SE, Francis JM, Robson MD, Neubauer S. Normal human left and right ventricular and left atrial dimensions using steady state free precession magnetic resonance imaging. J Cardiovasc Magn Reson 2005;7:775-782.

13. Lorenz CH, Walker ES, Morgan VL, Klein SS, Graham TP, Jr. Normal human right and left ventricular mass, systolic function, and gender differences by cine magnetic resonance imaging. J Cardiovasc Magn Reson 1999;1:7-21.
14. Bland JM, Altman DG. Statistical methods for assessing agreement between two methods of clinical measurement. Lancet 1986;1:307-310.
15. Selvanayagam J, Westaby S, Channon K, Francis J, Eichhofer J, Saito S, et al. Images in cardiovascular medicine. Surgical left ventricular restoration: an extreme case. Circulation 2003;107:e71.
16. Danilouchkine MG, Westenberg JJ, de Roos A, Reiber JH, Lelieveldt BP. Operator induced variability in cardiovascular MR: left ventricular measurements and their reproducibility. J Cardiovasc Magn Reson 2005;7:447-457.

Table 1: LV measurements in 21 healthy subjects

	7/3mm	7/0mm	6/4mm	P value
Ejection fraction (%)	67.2 ± 6.0 (64.5-70.0)	67.4 ± 5.3 (65.0-69.8)	69.2 ± 5.7 (66.6-71.8)	0.07
Mass (g)	119.8 ± 32.4 (105.1-134.5)	122.2 ± 34.0 (106.6-137.7)	119.8 ± 33.6 (104.5-135.1)	0.35
End-diastolic volume (ml)	155.8 ± 34.0 (140.3-171.2)	159.7 ± 36.3 (143.2-176.2)	157.8 ± 34.7 (142.1-173.6)	0.10
End-systolic volume (ml)	50.6 ± 12.9 (44.8-56.5)	52.3 ± 16.0 (45.0-59.6)	48.2 ± 12.3 (42.6-53.8)	0.05
Stroke volume (ml)	105.1 ± 27.0 (92.8-117.4)	107.4 ± 24.4 (96.3-118.5)	109.7 ± 27.5 (97.2-122.2)	0.14

Values are expressed as Mean ± SD (95% confidence interval); ANOVA was used to test for differences for continuous parameters among the three sequences; $p<0.05$ is statistically significant.

Table 2: Variability of left ventricular measurements

	Intraobserver		Interobserver		Interstudy	
	Bias (95% limits of agreement)	**CoV**	**Bias (95% limits of agreement)**	**CoV**	**Bias (95% limits of agreement)**	**CoV**
Ejection Fraction (%) 7/3mm	1.36 ± 3.43 (-5.36-8.08)	5.3	-2.75 ± 1.78 (-6.24-0.75)	2.8	2.06 ± 4.97 (-7.67-11.80)	7.8
Ejection Fraction (%) 7/0mm	3.14 ± 5.78 (-8.19-14.47)	9.1	-1.54 ± 2.91 (-7.24-4.15)	4.6	2.36 ± 5.40 (-8.22-12.95)	8.4
Ejection Fraction (%) 6/4mm	0.43 ± 2.49 (-4.45-5.31)	3.7	-1.19 ± 4.67 (-10.35-7.97)	7.2	2.47 ± 4.48 (-6.32-11.26)	6.8
Mass (g) 7/3mm	4.26 ± 6.67 (-8.80-17.33)	5.6	5.63 ± 10.28 (-14.51-25.77)	9.0	4.71 ± 12.21 (-19.23-28.65)	10.3
Mass (g) 7/0mm	1.67 ± 6.94 (-11.93-15.27)	5.8	9.07 ± 7.53 (-5.69-23.82)	6.5	-0.74 ± 10.72 (-21.75-20.26)	8.9
Mass (g) 6/4mm	4.18 ± 4.95 (-5.51-13.88)	4.2	4.93 ± 9.54 (-13.77-23.63)	8.3	2.21 ± 14.85 (-26.90-31.32)	12.5
End-diastolic volume (ml) 7/3mm	-6.61 ± 9.14 (-24.52 – 11.30)	6.9	10.17 ± 6.57 (-2.70-23.04)	4.6	-0.73 ± 12.62 (-25.48 – 24.01)	8.5
End-diastolic volume (ml) 7/0mm	-6.45 ± 8.15 (-22.42 – 9.53)	5.3	13.17 ± 8.13 (-2.77-29.10)	5.6	-1.97 ± 14.22 (-29.83 – 25.89)	9.5
End-diastolic volume (ml) 6/4mm	-5.73 ± 7.56 (-20.54 - 9.09)	5.0	13.09 ± 15.05 (-16.41-42.59)	10.6	0.10 ± 18.98 (-37.10 – 37.29)	12.8

Values are expressed as Mean ± SD (95% confidence interval); CoV= coefficient of variability; Mean and confidence interval determined according to the Bland and Altman method [14].